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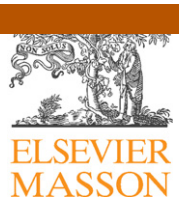

CLINICAL RESEARCH

Universal reperfusion therapy can be implemented: Lessons from 20 years of management of patients admitted within 6 hours of symptom onset with ST-segment elevation acute myocardial infarction

Reperfusion « pour tous » en phase aiguë d'infarctus du myocarde admis au cours des six premières heures : à propos de 20 ans d'expérience monocentrique

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KEYWORDS
Myocardial infarction;
Thrombolysis;

Summary
Aim. — To describe longitudinal trends in patients' characteristics, management and hospital outcomes over 20 years of therapy for ST-segment elevation myocardial infarction (STEMI).

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Primary angioplasty;
Glycoprotein IIb/IIIa inhibitors;
Stents

Methods. — From 1988 to 2007, 2100 consecutive patients with STEMI were admitted within 6 hours of symptom onset to a centre with a systematic reperfusion policy. The population was divided into three periods 1988—1996, 1996—2001 and 2001—2007.
Results. — The baseline risk of mortality increased over time ($p = 0.02$). Use of primary PCI increased and the proportion not receiving reperfusion therapy decreased (from 11.4 to 4.2%, $p = 0.0001$). Adjunctive use of stents and glycoprotein IIb/IIIa antagonists increased. The proportion of patients achieving acute TIMI-3 flow in the infarct artery increased (81 to 92%, $p = 0.001$), while time from symptom onset to reperfusion decreased (240 to 205 min, $p < 0.0001$). This was associated with a decrease in age- and sex-adjusted in-hospital mortality from 8.9 to 7.7% and eventually 5.4% ($p < 0.01$). However, the mortality of patients with cardiogenic shock was unaffected (76, 62 and 61%, respectively, $p = 0.18$).
Conclusion. — Reperfusion therapy can be implemented in up to 96% of STEMI patients admitted within 6 hours of symptom onset and this is associated with improvements in outcomes. Further improvements are needed in the management of patients with cardiogenic shock.

MOTS CLÉS
Infarctus du myocarde ;
Fibrinolyse ;
Angioplastie primaire ;
Inhibiteurs des récepteurs GP IIb/IIIa ;
Stents coronaires

Résumé
Objectifs. — Décrire l'évolution dans le temps des caractéristiques cliniques des patients, les modifications dans l'usage des techniques de reperfusion et leur impact sur les événements cardiovasculaires majeurs au cours de l'infarctus aigu du myocarde admis au cours des six premières heures.
Méthodes et résultats. — De 1988 à 2007, 2100 patients ont été admis consécutivement pour infarctus aigu du myocarde au cours des six premières heures. La population a été scindée en trois périodes : 1988—1996, 1996—2001 et 2001—2007 correspondant chacune à un groupe de 700 patients. Le risque global de chaque cohorte augmente avec le temps ($p = 0,02$). L'utilisation de l'angioplastie primaire augmente alors que le pourcentage de patients ne recevant pas de traitement de reperfusion diminue avec le temps (de 11,4 à 4,2 %, $p = 0,0001$). L'utilisation des stents et des inhibiteurs des récepteurs GP IIb/IIIa augmente. Le pourcentage de patients obtenant un flux TIMI 3 en phase aiguë augmente (81 à 92 %, $p = 0,001$), avec dans le même temps une diminution du temps entre le début de la douleur et la reperfusion effective (240 à 205 minutes, $p < 0,0001$). La mortalité hospitalière ajustée sur le sexe et l'âge diminue de 8,9 à 7,7 % et finalement 5,4 % pour la dernière période ($p < 0,01$). Cependant, la mortalité des patients admis en choc cardiogénique est restée inchangée (76, 62 et 61 %, $p = 0,18$).
Conclusion. — Un traitement de reperfusion a pu être appliqué à 96 % des patients admis au cours de six premières heures d'un infarctus du myocarde, permettant d'obtenir une réduction de la mortalité hospitalière. Au cours du choc cardiogénique, la stratégie idéale de prise en charge reste à définir.

Introduction

The management of ST-segment elevation acute myocardial infarction (STEMI) has evolved over the past 20 years towards widespread and timely implementation of reperfusion therapy for all patients admitted within 12 hours of symptom onset. Unfortunately, in large-scale cohort studies, approximately one-third of patients fail to receive reperfusion therapy despite being admitted within the first 12 hours and with electrocardiographic (ECG) ST-segment elevation qualifying them for early reperfusion [1,2]. The proportion of patients who are denied reperfusion therapy is even higher in the elderly population (up to 50% beyond 75 years of age) despite the fact that these individuals are at higher risk for early mortality. Even for patients receiving reperfusion therapies (either primary coronary angioplasty or intravenous fibrinolysis), delays to implementation are often longer than recommended [3,4].

Approximately 20 years ago, in 1988, we set up a policy of ''universal reperfusion therapy'' for patients with acute myocardial infarction (MI) with ST-segment elevation or new or presumed new left bundle branch block admitted within 6 hours of symptom onset [5]. The present study aims to describe the longitudinal changes in the clinical characteristics of our patients and to analyse the changes in implementation of, and type of, reperfusion therapies as well as their impact on hospital outcomes from 1988 to 2007.

Methods

Patient population

From June 1988 to June 2007, 2100 consecutive unselected patients with STEMI admitted less than 6 hours after symp-

tom onset were treated according to a previously described patency-oriented strategy [6]:

- primary coronary angioplasty if contraindications to fibrinolysis were present (patients at high risk of bleeding), uncertain diagnosis, cardiogenic shock or ideal conditions for primary percutaneous coronary intervention (PCI), i.e. immediate availability of the catheterization laboratory permitting timely reperfusion. These patients were admitted directly to the catheterization laboratory;
- pre- or in-hospital intravenous fibrinolysis, using accepted protocols, followed by routine 90-min emergency coronary angiography to ascertain the patency of the infarct-related artery. If the flow was TIMI grade 2 or 0-1, rescue angioplasty was usually attempted (except for patients randomized to clinical trials of rescue PCI or for those with small vessels). For patients with TIMI flow grade 3 in the infarct-related artery on emergency angiography, our policy evolved gradually from routine medical management during the first years to allowing, according to operator judgement, immediate angioplasty of the infarct artery;
- conservative medical therapy was reserved for the small subset of patients with advanced comorbidities, limited life expectancy and contraindications to both fibrinolysis and vascular access.

Modalities of admission were as follows: prehospital care in a mobile intensive care unit, transfer from the emergency room or another hospital, MI occurring during hospital stay, or another modality. The diagnosis of acute MI was based on conventional criteria: chest pain lasting more than 30 min and resistant to nitrates, with typical ECG changes ($\geq$ 1-mV ST-segment elevation in two or more limb leads or $\geq$ 2-mV ST-segment elevation in two or more contiguous precordial leads on a 12-lead electrocardiogram). A small subset of patients had typical chest pain but atypical ECG changes: minor ST-segment elevation, giant T waves, left bundle branch block, or accessory pathways. The diagnosis of MI was eventually confirmed in every case by the presence of elevated creatine kinase (above twice the upper limit of normal). Angiographic patency was defined as TIMI grade 3 flow in the infarct-related vessel. Multivessel disease was defined as the presence of greater or equal to 50% lumen diameter stenosis in at least two major epicardial arteries. The diagnosis of cardiogenic shock was based on the combination of systolic blood pressure of less or equal to 80 mmHg despite volume expansion and treatment with inotropic drugs, signs of acute circulatory failure (cyanosis, cold extremities, restlessness, mental confusion or coma) and congestive heart failure. All patients received at least 250 mg of intravenous aspirin and 4000 IU of unfractionated heparin (UFH), more frequently in the emergency department or in the prehospital mobile intensive care unit. Subsequently, intravenous UFH was given for at least 48 hours (starting at 1000 IU/h), adjusted to an activated partial thromboplastin time two to three times the control levels. Unless otherwise indicated (atrial fibrillation, left ventricular wall mural thrombus), treatment with UFH was stopped after catheterization if angioplasty of the infarct-related artery was performed during the acute phase. More recently, patients received clopidogrel (loading dose 300 mg) before admission regardless of the reperfusion modality (fibrinolysis or primary PCI); enoxaparin is now given in combination with tenecteplase according to the results of the Enoxaparin and Thrombolysis Reperfusion for Acute MI Treatment (EXTRACT) trial [7]. Until recently, abciximab was administered before admission in the catheterization laboratory for patients scheduled for primary PCI and the infusion was followed over the next 12 hours [8]. The combination of fibrinolysis (half dosage) and glycoprotein IIb/IIIa inhibitors was restricted to a few patients included in specific trials (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries [GUSTO] V) [9]. Bare-metal stents were used exclusively for emergency coronary angioplasty, and drug-eluting stents were implanted only in the setting of randomized trials (Trial to Assess the Use of the Cypher Stent in Acute MI Treated With Angioplasty, Typhoon, trial) [10].

For all patients, clinical, angiographic and outcome data were collected prospectively and entered into a database. In particular, the various delays were collected in real-time. For the purpose of this study, we collected 'door-to-recanalization time', defined as door to TIMI-3 flow for patients achieving reperfusion.

Statistical analysis

The population was divided in three equal groups of 700 patients each, corresponding to three periods, June 1988 to April 1996, May 1996 to May 2001 and June 2001 to June 2007. Trends in baseline characteristics were compared using a Cochran-Armitage trend test for categorical variables. All continuous variables are expressed as median and range or interquartile interval, and intergroup comparisons were performed using one-way ANOVA. When significant differences were found in the global comparisons among three groups, pair-wise comparisons were made with the Tukey-Kramer test.

A risk score for in-hospital mortality was computed from the baseline characteristics of the whole population. We first performed a bivariate analysis using Chi^2 and Student's t tests to determine the factors predictive of in-hospital mortality. Secondly, multivariable analysis was performed using a stepwise linear logistic regression. Variables included at this stage were those significantly linked to mortality in the bivariate analysis and the final model retained 5% significant variables using the Wald test.

The goodness-of-fit of the final model was assessed using the Hosmer-Lemeshow method (the samples were ranked according to their calculated risk; they were divided into ten equally sized classes; and, finally, the distribution of observed and expected numbers of deaths were compared using the Chi^2 test with eight degrees of freedom). The non-parametric comparison of risks between the three periods was made using the Kruskall-Wallis test.

All tests were two-tailed; a p-value < 0.05 was considered significant and all analyses were performed using the SAS statistical package (SAS Institute, North Carolina).

Table 1 Patients' baseline characteristics ($n = 2100$).

	1988–1996 ($n = 700$)	1996–2001 ($n = 700$)	2001–2007 ($n = 700$)	p value for trend
Median age, years (IQR)	58(25–91)	58(26–102)	57(21–99)	0.73
Patients aged > 70 years (%)	19.4	23.2	19.6	0.94
Median time from pain to admission, min (IQR)	180(120–240)	180(120–240)	160(120–240)	0.04
Women (%)	18.6	18.7	17.1	0.48
Anterior MI (%)	50.9	44.6	44.4	0.01
Risk factors (%)				
Hypertension	35.8	32.3	36.3	0.84
Diabetes	12.7	14.3	14.9	0.24
Dyslipidemia	41.6	36.7	35.4	0.02
Family history of CAD	30.6	31.3	26.0	0.06
Smoker	71.4	61.9	58.3	0.001
Previous CABG (%)	2.3	2.1	2.1	0.85
Previous PTCA (%)	3.4	6.4	9.9	0.001
Previous MI (%)	11.6	10.4	7.9	0.02
Ventricular fibrillation before admission (%)	4.0	5.3	8.6	0.001
Cardiogenic shock at admission (%)	5.3	4.6	5.1	0.90
MI due to stent thrombosis (%)	0	1.7	2.9	–
Multivessel disease (%)	43.3	45.4	45.1	0.51

CABG: coronary artery bypass graft; CAD: coronary artery disease; IQR: interquartile range; MI: myocardial infarction; PTCA: percutaneous transluminal coronary angioplasty.

Results

Baseline characteristics

The baseline clinical characteristics of the patients in the three cohorts are summarized in Table 1 . Over time, while the age and sex distribution remained stable, there were fewer smokers (from 71.4% in the initial cohort to 61.9% and 58.3% for the latest cohort, $p < 0.001$) and fewer patients with a previous or anterior MI. There were more patients with a history of ventricular fibrillation before admission. Conversely, the proportion of patients admitted with cardiogenic shock remained stable (5%). The time from pain to admission decreased from 180 to 160 min ($p = 0.04$). There was a continuous increase in the proportion of patients with a history of coronary angioplasty (currently close to 10%), while the proportion with a history of coronary bypass surgery remained stable (2%). The proportion of patients with multivessel disease was similar across the three periods. In the latest period, 20 of 700 patients (2.9% of all STEMI patients) were admitted for an infarction complicating stent thrombosis.

Modalities and results of acute reperfusion

The various types of reperfusion therapy and adjunctive antithrombotic therapies are summarized in Table 2. The use of intravenous fibrinolysis decreased steadily over time and was in the latest period confined to prehospital administration, which accounts for the reduction in time from symptom onset to administration of fibrinolytic therapy (from 172 to 144 min, $p = 0.0001$). Rescue PCI was performed in approximately one-quarter of patients treated with fibrinolysis throughout the observation period.

In parallel with the reduction in use of fibrinolytic therapy, there was an increase in the use of primary PCI, which was used in more than two-thirds of patients in the latest period. For patients undergoing primary PCI, the median door-to-reperfusion time decreased, from 50 to 45 and 40 min ($p = 0.0001$). The increasing use of primary PCI was associated with a reduction in the proportion of patients failing to receive reperfusion therapy, which decreased from 11.4 to 4.2% ($p = 0.0001$). Overall, 88.6, 91.0 and 95.8% of patients received acute reperfusion therapy over the three consecutive periods ($p = 0.001$). In addition to increasing implementation of reperfusion therapy, adjunctive therapy also evolved, with a substantial increase in the use of stents (from 3.9 to 79.4%) and intravenous glycoprotein IIb/IIIa receptor antagonists (from 1 to 87%; exclusively abciximab in this setting), both of which dramatically increased in the setting of primary PCI ($p < 0.0001$ for both).

On the whole, the proportion of patients with successful coronary recanalization, i.e. those with angiographically-proven TIMI-3 flow in the infarct-related artery, steadily increased over the three periods, from 81 to 87 to 92% ($p = 0.001$), with a shorter median time from onset of chest pain to infarct-artery recanalization (240, 230 and 205 min, respectively, $p < 0.0001$).

Table 2 Types of, delays to, and results of reperfusion therapy.

	1988-1996 ($n=700$)	1996-2001 ($n=700$)	2001-2007 ($n=700$)	*P* value for trend
Type of reperfusion therapy (%)				
Intravenous fibrinolysis	45.1	25.3	25.9	0.0001
Prehospital administration	53	50	90	–
Rescue angioplasty	25	26	28	–
Primary PCI	43.5	65.7	69.9	0.0001
No reperfusion	11.4	9.0	4.2	0.0001
Median delays to reperfusion therapy, min (IQR)				
Pain to fibrinolysis	172 (30—360)	165 (30—360)	144 (20—360)	0.0001
Door-to-recanalization in primary PCI	50 (30—60)	45 (30—60)	40 (30—60)	0.0001
Modalities of primary PCI (%)				
Glycoprotein IIb/IIIa inhibitors	1	32	87	0.0001
Coronary stents	3.9	48.1	79.4	0.0001
Global results on acute reperfusion (entire cohort)				
Successful acute reperfusion, TIMI 3 flow (%)	81	87	92	0.001
Median time from pain onset to TIMI 3 flow, min (IQR)	240(30—540)	230(55—780)	205(40—650)	0.0001

Table 3 Clinical outcomes.

Outcome	1988—1996 ($n=700$)	1996—2001 ($n=700$)	2001—2007 ($n=700$)	*p* value for trend
In-hospital mortality (%)				
All patients	8.9	7.7	5.4	0.01 [ok?]
In patients without cardiogenic shock	5.1	5.1	2.4	0.01
In patients with cardiogenic shock	76	62	61	0.18
Acute reocclusion of the IRA (%)	2.4	2.7	2.4	1.0
Vascular repair surgery (%)	0.7	0.2	0.4	0.41
Transfusion rate (%)	4	0.5	1	0.0001
Intracranial hemorrhage (%)	0.6	0.1	0.3	0.35
Cardiogenic shock developing during hospitalization (%)	2.6	2.0	1.4	0.13

IRA: infarct-related artery; NS: not significant.

Clinical outcomes

In-hospital mortality decreased from 8.9 to 7.7% and eventually to 5.4% ($p<0.01$; Table 3). While mortality decreased in the overwhelming majority (95%) of patients who presented without cardiogenic shock upon admission (from 5.1 to 2.4%, $p=0.01$), it remained essentially unchanged in the smaller group (5%) with cardiogenic shock (76, 62 and 61%, respectively, $p=0.18$). The percentage of patients developing cardiogenic shock during hospitalization was low with a favourable but non-significant trend between the three periods (Table 3). Mortality was remarkably consistent at 7% across subgroups defined according to the mode of admission of the patient (Fig. 1) with the exception of a marked increase in mortality for the small group of patients ($n=57$, 2.7% of the whole cohort) who developed acute MI while

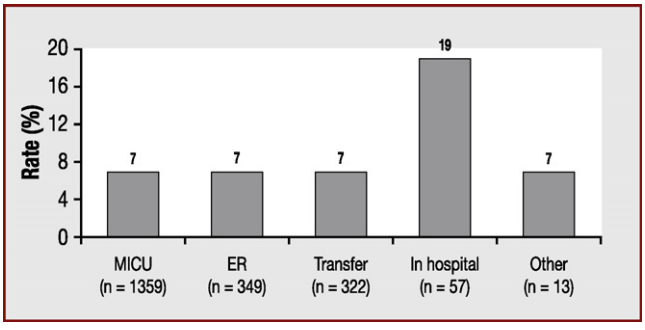

Figure 1. Hospital mortality according to admission modality. MICU: mobile intensive care unit; ER: emergency room.

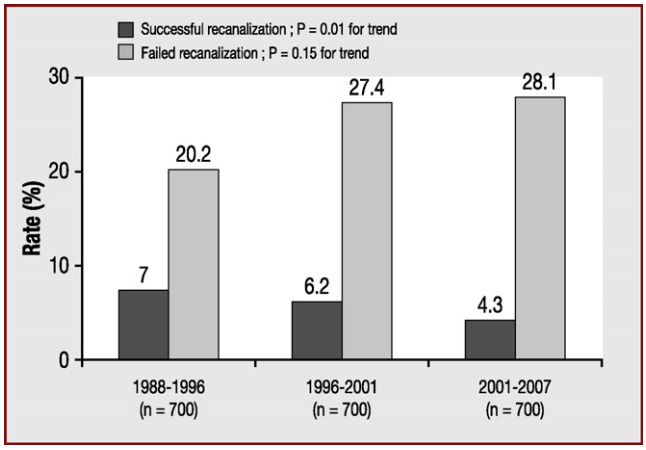

Figure 2. Hospital mortality in patients with or without successful recanalization.

hospitalized in another department, in whom hospital mortality was 19%. Hospital mortality rates in patients with or without successful recanalization are described in Fig. 2.

The observed mortality according to type of reperfusion therapy is shown in Fig. 3, with a 25% mortality for patients who failed to receive reperfusion therapy and lower in-hospital mortality for all other subsets. Among patients who received reperfusion therapy, mortality was lowest for those who had successful fibrinolysis (alone or with immediate PCI) or spontaneous reperfusion and was higher for patients who required rescue PCI or underwent primary PCI. For patients admitted with a prior cardiac arrest, mortality was much higher than for those without cardiac arrest (23.4% vs 6.33%, $p < 0.001$).

Acute symptomatic reocclusion of the infarct-related artery occurred during hospital stay at the same rate over the three periods (17, 19 and 17 patients, i.e. 2.5% of the patients required emergency coronary angioplasty). The rates of severe haemorrhagic complications, including intracranial haemorrhage, vascular surgery at the access site (mostly femoral), did not change across the three periods.

Risk score for in-hospital death

Using multivariable analysis, three factors were correlated with increased in-hospital mortality (increasing age, multivessel disease and cardiogenic shock upon admission) while

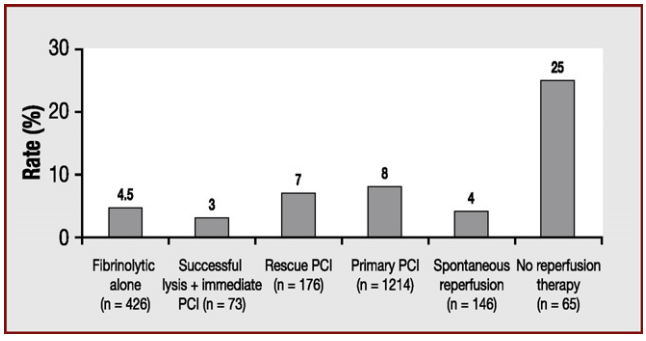

Figure 3. Hospital mortality according to type of reperfusion therapy.
PCI: percutaneous coronary intervention.

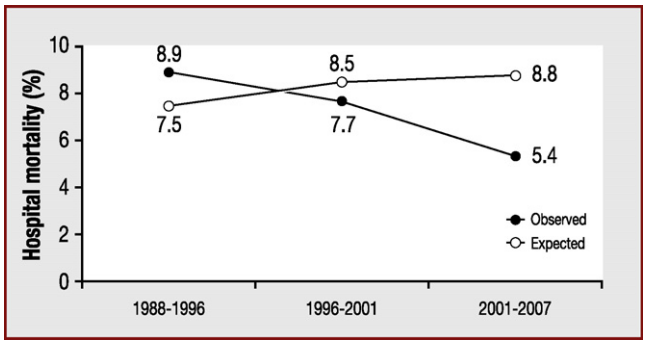

Figure 4. Observed and expected hospital mortality rates from 1988 to 2007.

two were associated with improved survival (active smoking and dyslipidaemia). Using these five predictors, the model had an excellent correlation between observed and expected in-hospital mortality rates (Hosmer and Lemeshow goodness-of-fit test: 0.9926). The non-parametric comparison of risk between the three periods (using the sum-of-scores methods) showed a continuous increase in baseline risk over time ($p = 0.02$).

Using the risk score, an 'expected' mortality was computed; the observed and expected in-hospital mortality rates are depicted in Fig. 4. There was a continuous and marked decrease in the ratio of observed to expected mortality from 1.19 to 0.91 and 0.61.

Discussion

With increasing use of primary PCI, it has been possible to offer reperfusion therapy to a greater proportion of patients with STEMI presenting within 6 hours of symptom onset, while improving time to reperfusion. We observed minor changes in the patients' baseline characteristics and their baseline mortality risk increased over time. Yet, through greater use of reperfusion therapy and improved adjunctive therapy, in-hospital mortality has decreased steadily. Despite these improvements, the mortality of patients admitted with cardiogenic shock remains alarmingly high, indicating that therapies beyond reperfusion will be needed to reduce the short-term mortality of cardiogenic shock.

There are several important aspects to these observations. The first concerns the feasibility of offering reperfusion therapy to virtually all patients with STEMI who present early. In the most recent cohort in our study, reperfusion therapy was provided to 96% of patients, a percentage well above that described in large multicentre series [2,11,12]. This was due largely to round-the-clock availability of primary PCI.

Second, overall mortality decreased steadily, which most likely reflects the combined effects of more frequent use of reperfusion therapy, increasing use of primary PCI over fibrinolysis [13], shortened delays to reperfusion, and improved adjunctive therapies such as stents, glycoprotein IIb/IIIa antagonists and thienopyridines [14–16]. The in-hospital mortality among patients without cardiogenic shock (who represent the overwhelming majority of the total cohort) is now well below 3%, a figure that will presumably be diffi-

cult to improve, indicating that short-term mortality in this patient group may very well have reached its nadir. This does not detract from the need to improve further post-discharge outcomes and disability, which remain substantial [17]. It also emphasizes the importance of non-fatal endpoints during the index hospital stay as important targets for improvement: prevention of bleeding, preservation of left ventricular function and treatment of heart failure. We have not collected all the medications administered during in-hospital stay. However, patients have received all the drugs according to the ongoing international guidelines since 1988: first beta-blockers, then angiotensin-converting enzyme inhibitors, followed with statin and aspirin plus clopidogrel for all patients. Also, continued efforts to reduce delays to first medical contact and subsequent delays to reperfusion are needed as these are directly correlated to 6-month mortality [18].

Third, and in contrast, it is noteworthy that the proportion of patients admitted with cardiogenic shock remained constant, at approximately 5%, and that in-hospital mortality in this patient subset exceeds 60%. The SHOCK (SHould we emergently revascularize Occluded Coronaries in cardiogenic shocK?) trial demonstrated substantial improvements in mortality with revascularization (using PCI or CABG) in this patient population, although this effect was observed mostly for post-discharge mortality, with little impact on in-hospital mortality [19—21]. This emphasizes the need for intensive further research on novel pathways to reduce mortality in this group of patients; whether this will be achieved by exploring novel pharmacological approaches [22] or by improved devices for circulatory support [23] remains unclear. However, prevention of cardiogenic shock may be equally important as treating it. In this regard, prior studies have demonstrated that prehospital fibrinolysis (as opposed to transfer to an interventional centre for primary PCI) is associated with a reduction in the incidence of cardiogenic shock, particularly if prehospital fibrinolysis is implemented in the first 2 to 3 hours after symptom onset [12,24], which argues for keeping prehospital fibrinolysis in the management algorithm for patients with STEMI seen very early.

Two additional aspects are noteworthy. The proportion of patients admitted for STEMI because of stent thrombosis represented a substantial group of almost 3% of all admissions in the cohort. Given the reports of an increased frequency of late stent thrombosis with drug-eluting stents compared to bare-metal stents [25—27] and the relatively low rate of use of drug-eluting stents at the time when this cohort was accrued, this proportion may very well increase further in the future, emphasizing that stent thrombosis is not a trivial problem [28]. Second, the proportion of patients admitted for STEMI following successful prehospital resuscitation for cardiac arrest is growing. This most likely reflects improvements in the prehospital care of these individuals. However, this group continues to experience high hospital mortality (23.4%), indicating that other issues beyond ensuring timely recanalization of the infarct-related artery need to be addressed in this very high-risk group.

Impact of admission modality on clinical outcome

The high mortality rate (19%) observed in the small subset of patients ($n = 57$) experiencing in-hospital MI while admitted in another department is worthy of further study. The role of delayed diagnosis and extracardiac comorbidities needs to be explored.

Impact of reperfusion type on clinical outcome

Differences in mortality between groups as a function of type of reperfusion therapy received should be interpreted with caution given the major differences in baseline characteristics and risk (Table 4), the type of adjunctive therapies, and the year of enrolment in these patient subsets. In particular, the very low mortality seen in patients with successful fibrinolysis followed by immediate angioplasty of the culprit vessel should be viewed with caution given the negative results of the facilitated angioplasty strategy in the Assess-

Table 4 Patients' baseline characteristics according to initial reperfusion modality ($n = 2100$).

	Primary angioplasty ($n = 1252$)	Intravenous fibrinolysis ($n = 673$)	Conservative medical therapy ($n = 175$)	p value for trend
Median age, years	59	56	63	0.0001
Median time from pain to admission, min	182	195	174	0.006
Women (%)	18	15	29	0.0001
Anterior MI (%)	46	47	48	0.87
Previous CABG (%)	3	0.7	1	0.002
Previous PTCA (%)	8	5	2	0.0002
Previous MI (%)	11	7	11	0.03
Cardiogenic shock at admission (%)	6	3	3	0.0009
Ventricular fibrillation before admission (%)	8	3	5	0.0008
Multivessel disease (%)	46	41	46	0.11

MI: myocardial infarction; CABG: coronary artery bypass graft; PTCA: percutaneous transluminal coronary angioplasty.

ment of the Safety and Efficacy of a New Thrombolytic agent (ASSENT)-4 PCI and Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) trials [29,30]. Results from the Combined Abciximab REteplase Stent Study in Acute MI (CARESS in AMI) and Trial of Routine ANgioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in Acute MI (TRANSFER-AMI) trials suggest that for patients receiving fibrinolytic therapy, PCI performed in the hours following may be a good option [31,32]. Indeed, in the recent French nationwide FAST-MI (French registry of Acute ST elevation or non-ST-elevation MI) registry, which enrolled patients over a 1-month period in November 2005, mortality was similar for patients treated with fibrinolysis (with liberal use of subsequent PCI) and for those treated with primary PCI [33]. This strategy of fibrinolysis and subsequent ''regimented'' PCI [34] using optimal pharmacological adjunctive therapy, is being compared prospectively to primary PCI in the ongoing Strategic Reperfusion Early After MI (STREAM) randomized trial. Most of the patients presenting with cardiogenic shock were treated with primary PCI, highlighting the higher rate of in-hospital mortality in this subset of PCI patients.

Comparison with historical registries

Overall, our data are consistent with those of similar experiences of long-term longitudinal surveys and registries of acute MI [35,36], which concur in demonstrating an increase in the use of reperfusion therapy and its long-term survival benefit [37]. The reduction in early mortality seen in our study is consistent with similar findings from the USIC 2000 [38] and FAST-MI French registries, and most likely reflects the impact of improved adjunctive pharmacological therapy. For example, in the German Acute COronary Syndromes (ACOS) registry, the combined use of clopidogrel and aspirin reduced the 1-year mortality rate from 10.4 to 6.1% in fibrinolyzed patients and from 10.9 to 6.4% in PCI-treated patients [39]. These findings emphasize that there is more to the management of acute STEMI than reperfusion therapy alone.

Limitations

These data are observational, and mirror the experience of a single centre. They do, however, reflect a consecutive unbiased population of patients with acute STEMI admitted within 6 hours of symptom onset, with careful and prospective collection of time intervals and outcomes.

Conclusions

There is an important lesson for clinical practice from this cohort: the recommendation to offer reperfusion therapy to all eligible candidates [3,4] can be implemented in clinical practice to almost all patients and reduce the proportion of non-reperfused patients to less than 5%. This is likely to have a substantial impact in reducing mortality in this frequent and deadly condition.

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